

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
 US Department of Commerce  
 United States Patent and Trademark  
 Office, PCT  
 2011 South Clark Place Room  
 CP2/5C24  
 Arlington, VA 22202  
 ETATS-UNIS D'AMERIQUE  
 in its capacity as elected Office

<b>Date of mailing (day/month/year)</b> 15 August 2001 (15.08.01)	<b>Applicant's or agent's file reference</b> ML/P32426
<b>International application No.</b> PCT/GB00/03747	<b>Priority date (day/month/year)</b> 01 October 1999 (01.10.99)
<b>International filing date (day/month/year)</b> 29 September 2000 (29.09.00)	
<b>Applicant</b> ABUIN, Alejandro et al	

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

30 April 2001 (30.04.01)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<b>The International Bureau of WIPO</b> 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	<b>Authorized officer</b> Zakaria EL KHODARY Telephone No.: (41-22) 338.83.38
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## PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

CONNELL, Anthony, Christopher  
GlaxoSmithKline  
Corporate Intellectual Property  
(CN9.25.1)  
980 Great West Road  
Brentford  
Middlesex TW8 9GS  
ROYAUME-UNI

Date of mailing (day/month/year) 01 March 2002 (01.03.02)	<b>IMPORTANT NOTIFICATION</b>
Applicant's or agent's file reference ML/P32426	
International application No. PCT/GB00/03747	International filing date (day/month/year) 29 September 2000 (29.09.00)

1. The following indications appeared on record concerning:		
<input type="checkbox"/> the applicant	<input type="checkbox"/> the inventor	<input checked="" type="checkbox"/> the agent
<input type="checkbox"/> the common representative		
Name and Address CONNELL, Anthony, Christopher Corporate Intellectual Property SmithKline Beecham Two New Horizons Court Brentford, Middlesex TW8 9EP United Kingdom	State of Nationality	State of Residence
	Telephone No. +44 127 964 4395	
	Facsimile No. +44 020 8975 6294	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:		
<input type="checkbox"/> the person	<input type="checkbox"/> the name	<input checked="" type="checkbox"/> the address
<input type="checkbox"/> the nationality		
<input type="checkbox"/> the residence		
Name and Address CONNELL, Anthony, Christopher GlaxoSmithKline Corporate Intellectual Property (CN9.25.1) 980 Great West Road Brentford Middlesex TW8 9GS United Kingdom	State of Nationality	State of Residence
	Telephone No. +44(0) 20 8047 5000	
	Facsimile No. +44(0) 20 8047 6894	
	Teleprinter No.	
3. Further observations, if necessary:		
4. A copy of this notification has been sent to:		
<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned	
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned	
<input type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:	

<b>The International Bureau of WIPO</b> 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Jaime LEITAO Telephone No.: (41-22) 338.83.38
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# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 11 JAN 2002

WIPO PCT

Applicant's or agent's file reference ML/P32426	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB00/03747	International filing date (day/month/year) 29/09/2000	Priority date (day/month/year) 01/10/1999
International Patent Classification (IPC) or national classification and IPC A01K67/027		
Applicant SMITHKLINE BEECHAM P.L.C.		



- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 5 sheets, including this cover sheet.
 

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

- This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 30/04/2001	Date of completion of this report 09.01.2002
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Trommsdorff, M Telephone No. +49 89 2399 7361 

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/03747

## I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

### Description, pages:

1-15 as originally filed

### Claims, No.:

1-16 as originally filed

### Drawings, sheets:

1/2-2/2 as originally filed

### Sequence listing part of the description, pages:

1-3, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/03747

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

### 1. Statement

Novelty (N)	Yes:	Claims	7, 8, 14-16
	No:	Claims	1-6, 9-13
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-16
Industrial applicability (IA)	Yes:	Claims	1-16
	No:	Claims	

2. Citations and explanations  
**see separate sheet**

**1. Cited documents**

The following documents (D) are referred to in this communication; the numbering is the same as in the search report and will be adhered to in the rest of the procedure:

- D1: WO 98 45438 A (LOWELL BRADFORD B ;FLIER JEFFREY S (US); BETH ISRAEL HOSPITAL (US)) 15 October 1998 (1998-10-15)  
D2: WO 99 10013 A (ROSENTHAL NADIA A ;UNIV PENNSYLVANIA (US); SWEENEY H LEE (US); MAS) 4 March 1999 (1999-03-04)

**2. Re Item V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventiv step or industrial applicability; citations and explanations supporting such statement**

- 2.1. The claims are directed to a transgenic rodent expressing a human UCP3 polypeptide, to a method for producing said rodent and to methods of using said rodent.

D1 discloses the nucleic and amino acid sequences of UCP3 (seq. ID no 2 and 3, respectively). Also described are knockout animals, such as mice, which lack UCP3 and transgenetically overexpress UCP3 (p.26, l.33-p.27, l.12).

Thus, the teaching of D1 is novelty destroying to the subject-matter of claims 1-6 and 9-13 (Art. 33(2) PCT).

- 2.2. Claims 15 and 16 are directed to a method of determining the phenotypic effect of a compound by exposing said transgenic rodent to said compound.

D1 states that treatment of rats with Intralipid plus heparin causes a 3-fold increase in UCP3 and shows that nicotinic acid treatment of fasted animals increases UCP3 mRNA levels 2-fold compared to fasted controls. D1 further suggests that UCP3 is linked to protein catabolism in skeletal muscle (p.38, example 5).

The difference between the claims and D1 resides in that in D1 the animal treated are not transgenic animal. However, the problem solved is the same as in the application, i.e. analysing the effect of different compounds on UCP3. Moreover, D1 suggests that "the overexpression of UCP3 (e.g., human UCP3) in transgenic mice can be used as a means of creating a test system for UCP3 activators and

inhibitors". Thus, since the application merely describes an alternative method to obtain the same result, no inventive step can be seen for the subject-matter of claims 15 and 16 (Art. 33(3) PCT).

- 2.3. Claims 7, 8 and 14 are directed to a transgenic rodent wherein UCP3 is expressed under the control of a muscle specific promoter, such as the alpha-actin promoter and to said transgene.

As mentioned above, D1 describes transgenic rodents expressing UCP3. Said transgenic rodents only differ from the claimed animals in that no specific promoter is mentioned. However, D1 further mentions that "in humans, UCP3 is expressed abundantly and preferentially in skeletal muscle" (p.38, l.9-11). Since, the skeletal muscle is the tissue where UCP3 is naturally expressed, it seems obvious to use a transgene with a promoter which favours UCP3 expression in muscle. Muscle specific promoters are known in the art and extensively described. D2, for instance, cites several muscle specific promoters such as, e.g., the myosin light chain 1/3 promoter/enhancer, the skeletal alpha-actin promoter, etc. (p.6, l.4-8) and gives the example of transgenic animals expressing IGF-I under the control of the MLC 1/3 promoter/enhancer sequence (p.22, example 1).

Hence, the subject-matter of claims 7, 8 and 14 lacks an inventive step (Art. 33(2) PCT).

- 2.4. The subject-matter of claims 1-16 is industrially applicable in the field of pharmaceutical industry (Art. 33(4) PCT).

# INTERNATIONAL SEARCH REPORT

Int Application No  
PCT/GB 00/03747

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 A01K67/027 C12N15/12 C07K14/47

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 A01K C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)  
EPO-Internal, WPI Data, PAJ, MEDLINE, BIOSIS

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 45438 A (LOWELL BRADFORD B ;FLIER JEFFREY S (US); BETH ISRAEL HOSPITAL (US)) 15 October 1998 (1998-10-15)	1-6, 9-13,15, 16
Y	page 26, line 33 -page 27, line 7 example 5	7,8,14
Y	WO 99 10013 A (ROSENTHAL NADIA A ;UNIV PENNSYLVANIA (US); SWEENEY H LEE (US); MAS) 4 March 1999 (1999-03-04) page 5, line 26 -page 6, line 10 page 25, line 4 - line 5	7,8,14

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*G\* document member of the same patent family

Date of the actual completion of the international search

22 February 2001

Date of mailing of the international search report

13/03/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Mandl, B



# INTERNATIONAL SEARCH REPORT

Int. Application No  
PCT/GB 00/03747

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BOSS O. ET AL.: "THE UNCOUPLING PROTEINS, A REVIEW" EUROPEAN JOURNAL OF ENDOCRINOLOGY, vol. 139, no. 1, 1998, pages 1-9, XP000916888 ISSN: 0804-4643 page 5	1-20
A	STEFL B. ET AL.: "Brown fat is essential for cold-induced thermogenesis but not for obesity resistance in aP2-Ucp mice." AMERICAN JOURNAL OF PHYSIOLOGY, vol. 274, no. 3 PART 1, March 1998 (1998-03), pages E527-E533, XP002161151 ISSN: 0002-9513 the whole document	1-20

# INTERNATIONAL SEARCH REPORT

Information on patent family members

Int. Application No

PCT/GB 00/03747

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9845438 A	15-10-1998	AU 7466198 A	30-10-1998
WO 9910013 A	04-03-1999	AU 9293598 A	16-03-1999

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>ML/P32426</b>	<b>FOR FURTHER ACTION</b> <small>see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.</small>	
International application No. <b>PCT/GB 00/ 03747</b>	International filing date ( <i>day/month/year</i> ) <b>29/09/2000</b>	(Earliest) Priority Date ( <i>day/month/year</i> ) <b>01/10/1999</b>
Applicant  <b>SMITHKLINE BEECHAM P.L.C.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☒ contained in the international application in written form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

**TRANSGENIC RODENT COMPRISING A POLYNUCLEOTIDE ENCODING A HUMAN UCP3 POLYPEPTIDE**

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

## INTERNATIONAL SEARCH REPORT

International Application No

PC 03 00/03747

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A01K67/027 C12N15/12 C07K14/47

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A01K C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, MEDLINE, BIOSIS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 45438 A (LOWELL BRADFORD B ;FLIER JEFFREY S (US); BETH ISRAEL HOSPITAL (US)) 15 October 1998 (1998-10-15)	1-6, 9-13,15, 16
Y	page 26, line 33 -page 27, line 7 example 5	7,8,14
Y	--- WO 99 10013 A (ROSENTHAL NADIA A ;UNIV PENNSYLVANIA (US); SWEENEY H LEE (US); MAS) 4 March 1999 (1999-03-04) page 5, line 26 -page 6, line 10 page 25, line 4 - line 5 --- -/--	7,8,14

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

22 February 2001

Date of mailing of the international search report

13/03/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Mandl, B

# INTERNATIONAL SEARCH REPORT

International Application No

PC 00/03747

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BOSS O. ET AL.: "THE UNCOUPLING PROTEINS, A REVIEW" EUROPEAN JOURNAL OF ENDOCRINOLOGY, vol. 139, no. 1, 1998, pages 1-9, XP000916888 ISSN: 0804-4643 page 5	1-20
A	STEFL B. ET AL.: "Brown fat is essential for cold-induced thermogenesis but not for obesity resistance in aP2-Ucp mice." AMERICAN JOURNAL OF PHYSIOLOGY, vol. 274, no. 3 PART 1, March 1998 (1998-03), pages E527-E533, XP002161151 ISSN: 0002-9513 the whole document	1-20

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PC7 8 00/03747

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9845438	A	15-10-1998	AU	7466198 A	30-10-1998
WO 9910013	A	04-03-1999	AU	9293598 A	16-03-1999

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

## PCT

To:  
GlaxoSmithKline  
Corporate Intellectual Property  
Attn. Connell, Anthony C.  
Two New Horizons Court  
Brentford  
Middlesex TW8 9EP  
UNITED KINGDOM

**RECEIVED**  
2 MAR 2001  
NEW HORIZONS COURT

NOTIFICATION OF TRANSMITTAL OF  
INTERNATIONAL SEARCH REPORT  
OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference <b>ML/P32426</b>	Date of mailing (day/month/year) <b>13/03/2001</b>
International application No. <b>PCT/GB 00/ 03747</b>	International filing date (day/month/year) <b>29/09/2000</b>
Applicant  <b>SMITHKLINE BEECHAM P.L.C.</b>	

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

**Filing of amendments and statement under Article 19:**  
The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

**Where?** Directly to the International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland  
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority European Patent Office, P.B. 5818 Patentaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer  <b>Carla Louro</b>
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## NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

#### What parts of the International application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

#### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

#### How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

#### What documents must/may accompany the amendments?

##### Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.



## NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:  
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:  
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:  
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or  
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:  
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

### "Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

### Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

### Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

# INTERNATIONAL COOPERATION TREATY

## PCT

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>ML/P32426</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/GB 00/ 03747</b>	International filing date (day/month/year) <b>29/09/2000</b>	(Earliest) Priority Date (day/month/year) <b>01/10/1999</b>
Applicant  <b>SMITHKLINE BEECHAM P.L.C.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☒ contained in the international application in written form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

**TRANSGENIC RODENT COMPRISING A POLYNUCLEOTIDE ENCODING A HUMAN UCP3 POLYPEPTIDE**

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

# INTERNATIONAL SEARCH REPORT

National Application No  
PCT/GB 00/03747

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 A01K67/027 C12N15/12 C07K14/47

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A01K C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, MEDLINE, BIOSIS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 45438 A (LOWELL BRADFORD B ;FLIER JEFFREY. S (US); BETH ISRAEL HOSPITAL (US)) 15 October 1998 (1998-10-15)	1-6, 9-13,15, 16
Y	page 26, line 33 -page 27, line 7 example 5	7,8,14
Y	WO 99 10013 A (ROSENTHAL NADIA A ;UNIV PENNSYLVANIA (US); SWEENEY H LEE (US); MAS) 4 March 1999 (1999-03-04) page 5, line 26 -page 6, line 10 page 25, line 4 - line 5	7,8,14
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

22 February 2001

Date of mailing of the international search report

13/03/2001

Name and mailing address of the ISA

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Mandl, B

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/03747

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BOSS O. ET AL.: "THE UNCOUPLING PROTEINS, A REVIEW" EUROPEAN JOURNAL OF ENDOCRINOLOGY, vol. 139, no. 1, 1998, pages 1-9, XP000916888 ISSN: 0804-4643 page 5	1-20
A	----- STEFL B. ET AL.: "Brown fat is essential for cold-induced thermogenesis but not for obesity resistance in aP2-Ucp mice." AMERICAN JOURNAL OF PHYSIOLOGY, vol. 274, no. 3 PART 1, March 1998 (1998-03), pages E527-E533, XP002161151 ISSN: 0002-9513 the whole document -----	1-20

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 00/03747

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9845438 A	15-10-1998	AU 7466198 A	30-10-1998
WO 9910013 A	04-03-1999	AU 9293598 A	16-03-1999

## (12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



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12 April 2001 (12.04.2001)

PCT

(10) International Publication Number  
**WO 01/24625 A1**

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- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
9923334.8 1 October 1999 (01.10.1999) GB
- (71) Applicant (for all designated States except US):  
SMITHKLINE BEECHAM P.L.C. [GB/GB]; New Horizons Court, Brentford, Middlesex TW8 9EP (GB).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): ABUIN, Alejandro [ES/GB]; SmithKline Beecham Pharmaceuticals, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). CLAPHAM, John [GB/GB]; SmithKline Beecham Pharmaceuticals, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB).
- (74) Agent: CONNELL, Anthony, Christopher; Corporate Intellectual Property, SmithKline Beecham, Two New Horizons Court, Brentford, Middlesex TW8 9EP (GB).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- Published:**
- With international search report.
  - Before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: TRANSGENIC RODENT COMPRISING A POLYNUCLEOTIDE ENCODING A HUMAN UCP3 POLYNUCLEOTIDE

(57) Abstract: A transgenic mouse expressing human uncoupling protein 3 (UCP) is disclosed, together with methods of preparation and the uses thereof.

WO 01/24625 A1